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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/685,925	10/15/2003	Dwight L. Anderson	110.01840101	7050

26813 7590 05/11/2007
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EXAMINER
LUCAS, ZACHARIAH

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
05/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/685,925	**Applicant(s)** ANDERSON ET AL.
	Examiner Zachariah Lucas	**Art Unit** 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _12 February 2007_.
2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-9 and 13-17_ is/are pending in the application.
  4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) _1-9 and 13-17_ is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
  Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. 5/17/07
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-9, and 13-17 are pending and under consideration.

2. In the prior action, mailed on November 13, 2006, claims 1-9 and 13-19 were pending and rejected.

In the Response of February 12, 2007, claims 18 and 19 were cancelled from the application, and claims 1, 5, 13, and 15-17 were amended.

Prior Rejections- Withdrawn

3. **(Prior Rejection- Withdrawn)** Claims 1-6, 16, and 18 were rejected under 35 U.S.C. 102(e) as being anticipated by Madonna et al. (U.S. 2004/0224359- cited in the November 2005 IDS). The Applicant has amended the claims to require that the bacteriophage comprising a binding agent is immobilized to a substrate, or to require that the parent bacteriophage are removed prior to the incubation step and the release of the progeny phage from the target cells. In view of the amendments, the rejection is withdrawn.

4. **(Prior Rejections- Withdrawn)** Claims 6 and 9 were rejected under 35 U.S.C. 103(a) as being unpatentable over Madonna as applied to claims 1-6 and 16 above, and further in view of the teachings of Terlesky et al. (U.S. 2004/0152085), Stroobant et al. (U.S. 2002/0090637), and Petersen et al. (U.S. 2002/0042125). Claims 7 and 8 were rejected under 35 U.S.C. 103(a) as being unpatentable over Madonna as applied to claims 1-6 above, and further in view of Teodorescu et al. (U.S. 4,797,363). Claims 13-15, 17, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable Madonna as applied to claims 1-6, 16, and 18 above, and further in view of

Wang et al. (U.S. 4,663,277). In view of the amendments to the claims such that Madonna no longer anticipates claims 1-6, 16, and 18, the obviousness rejection is likewise withdrawn.

Claim Objections

5. **(New Objection)** Claim 13 is objected to because of the following informalities: in the step of the claim beginning "removing the complexes of new bacteriophage and second substrate" it appears that the claim should read - - removing the second substrate comprising immobilized binding agent for the new bacteriophage, to which the new bacteriophage, if present, is complexed- - , and that the following step should read not on the detection of the complexes generally, but on the detection of new bacteriophage on the second substrate.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. **(New Rejection)** Claims 1-4, 6, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rees et al. (WO 92/02633) in view of Miller et al. (WO 01/09370- as translated in U.S. 2002/0127547). Claim 1 currently reads on a method for the detection of a bacterial cell in a sample comprising contacting a sample with a first bacteriophage having a binding agent, wherein that first bacteriophage is immobilized onto a substrate, incubating the

sample under conditions such that the target bacterial cells are infected, and if present, such that new progeny phage are produced which do not comprise the binding agent, removing the first phage, and detecting the progeny phage.

Rees teaches a method for the detection of bacterial cells comprising the use of bacteriophage. The method involves contacting a target sample with the parent phage, permitting the phage to infect the cells, killing or removing the parent phage, permitting the infected cells to produce progeny phage, and detecting the progeny phage. Pages 6-7. The reference teaches that the progeny phage may be visually detected through expression of an indicator gene in a reporter bacteria. Pages 7 and However, the reference does not teach the immobilization of the parent phage, or the removal of the parent phage after the release of progeny phage from the target cells.

Miller also teaches a method for the detection of bacteria using phage. This reference teaches the immobilization of the phage onto a support (such as a polymer material, in the form of plates, slides, filters, etc.) such that it will infect target bacteria it comes into contact with and injects the bacteria with the phage nucleic acid. See, translation in the '547 publication, page 2 paragraph [0017], and pages 3 paragraphs [0027] (respectively teaching the support structures on which the phage may be immobilized, and teaching that such immobilized phage are capable of injecting its nucleic acid into the target bacterium). Further, the reference indicates that where a sample is contacted with an immobilized phage, there is no stringent necessity to remove such from the sample prior to detection. Thus, it would have been apparent to those of ordinary skill in the art that immobilized phage may be removed at any point after infection of the target bacteria in the sample (if any). The reference also teaches that the phage may be indirectly immobilized to the support through use of (e.g.) a polypeptide, which in turn binds to the support. Such a polypeptide would be equivalent to the binding agents of the present claims.

In view of these teachings of Miller, it would have been obvious to those of ordinary skill in the art that the parent phage of Rees may be similarly immobilized. Those of ordinary skill in the art would have been motivated to use such a technique as the Rees reference indicates that the parent phage should be killed or removed, and the technique of Miller would result in a convenient means for the removal of the parent phage. Moreover, while the references do not specifically teach the removal of the parent phage after release of the progeny phage, because Miller indicates the immobilization of the parent phage renders the necessity of removing the parent phage prior to detection (and thus prior to the release of the progeny phage) moot, it would have been obvious to those of ordinary skill in the art that the immobilized phage could be effectively removed at any point after infection, before, during, or after the progeny phage are released.

The combined teachings of these references therefore render the claimed invention obvious.

8. **(New Rejection)** Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rees and Miller as applied to claims 1-4, 6, and 9 above, and further in view of Vafai (U.S. 5,824,319). Claims 7 and 8 further limit the method of claim 1 to embodiments wherein the progeny phage are detected using a fluorescent dye, and through visualization using a light microscope. The teachings of Rees and Miller have been described in part above. In addition to the use of the reporter bacteria described above, Rees additionally indicates that an

immunological assay may also be used for the detection of the progeny phage. Pages 15-16. However, the reference does not teach the specific use of the dye and visualization technique identified in claims 7 and 8.

Vafai teaches immunoassay methods for the detection of a virus. Columns 11-14. Among the methods disclosed is an assay where an antibody is conjugated to a fluorescent dye, which can then be detected through the use of light microscope. Column 13, lines 27-47. Because this reference teaches the use of such dyes and visualization techniques in immunoassay methods for the detection of viruses, it would have been obvious to those of ordinary skill in the art to use such assays for the detection of the bacteriophage (a type of virus) of Rees. Those of ordinary skill in the art would have had a reasonable expectation of success in such a adaptation of the immunoassays of Vafai as immunoassays are generally recognized as useful for the detection of target antigens, and for viruses, and as the Rees reference suggests the use of such a detection method for the bacteriophage produced in the method described therein.

The combined teachings of these references therefore render the claimed inventions obvious.

9. **(New Rejection)** Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rees in view of Miller as applied to claims 1-4, 6, and 9 above, and further in view of Vonk et al. (J Immunol Methods 137: 133-39). Claims 13 and 14 describe a method similar to that in claim 1, except that these claims additionally require that the progeny phage are detected by contacting the sample from which the parent phage have been removed with a second substrate comprising immobilized binding agent for the progeny phage (e.g., anti-phage

antibodies), removing the complexes of the second substrate/progeny phage, and detecting the presence of new phage on the second substrate.

The teachings of Rees in view of Miller have been described above. As indicated above, the teachings of these references suggest the portions of the claimed methods with respect to the use of the immobilized parent phage, and the use of an immunoassay for the detection of the progeny phage. However, the reference does not teach or suggest the detection of progeny phage using a second substrate having a binding agent for the new phage immobilized thereto.

Vonk teaches a method for the detection of a virus comprising the use of magnetic beads (a substrate) having antibodies against the virus conjugated (immobilized) thereto. Abstract. The reference teaches that such beads are added to the test sample, are incubated for sufficient time for the beads to form complexes with any present virus, and are then separated from the sample and assayed for the presence of the virus. From these teachings, it would have been obvious to those of ordinary skill in the art that such beads would be useful for the detection of viruses (including phages) in a sample generally. Moreover, because it would have been apparent to those of ordinary skill in the art that the beads would be capable of also binding to the parent phage immobilized on the first substrate, it would also have been obvious to those of ordinary skill in the art to remove the first substrate from the sample prior to the contacting the sample with the beads. Those of ordinary skill in the art would have had a reasonable expectation of success in the combination based on the suggestion on the Rees reference that an immunoassay be used for the detection of the progeny phage, and on the teaching of Vonk describing an immunoassay useful for the detection of viruses in a sample.

The combined teachings of these references therefore render the claimed methods obvious.

10. **(New Rejection)** Claims 5 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over, respectively, Rees and Miller as applied to claims 1-4, 6, and 9 above; or Rees and Miller in view of Vonk as applied to claims 13 and 14 above, and further in view of Sun et al. (J Indust Microbiol Biotechnol 25: 273-75). These claims further limit the claimed methods to embodiments wherein the binding agent of the first bacteriophage is biotin.

The teachings of Rees, Miller, and Vonk have been described above. While the Rees reference teaches the indirect immobilization of the parent phage on a first substrate through the use of a polypeptide that binds the support, the reference does not teach or suggest embodiments where that protein is biotin.

However, the Sun reference teaches methods involving the immobilization of phage onto a substrate. The reference teaches the biotinylation of the phage, such that the biotin will then react to streptavidin on the substrate, thereby immobilizing the phage thereto. Because Sun provides a method for the immobilization of a phage onto a substrate such that the phage will then be capable of binding a target bacterium (thus, facing a similar problem for the immobilization of a phage on a substrate as would be faced by those attempting to indirectly attach a phage to a substrate as suggested by Rees) it would have been obvious to those of ordinary skill in the art to have used the solution described in Sun for the immobilization of the first phage in Rees.

The combined teachings of these references therefore render the claimed methods obvious.

11. **(New Rejection)** Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Wilson (U.S. 5,985,596) in view of Olsvik et al. (Clin Microbiol Rev 7:43-54), Sun et al. (J Indust Microbiol Biotech 25: 273-75), and Vonk (supra). Claim 16 reads on a method similar to that of claim 1 above, except that, while the parent phage do comprise a binding agent, they are not initially immobilized on a substrate. Rather, the sample is contacted with a substrate comprising a ligand for the binding agent of the phage after the sample is contacted with the parent phage, but before the incubation of the infected cells and release of the progeny phage. Claim 17 includes the features of claim 16, and additionally requires the additional limitations of detecting the progeny phage as described in claim 13.

As was previously described (see, action mailed on December 16, 2004), Wilson teaches a method for the detection of bacterial cells comprising the steps of incubating a sample with a first bacterium, removing or inactivating the first bacterium, and detecting the formation of plaques in a bacterial culture, the presence of such plaques indicating the infection of cells in the sample, and therefore the presence of the target bacterial cells. Column 1. The reference teaches that such methods may be used for the detection of bacteria such a Salmonella spp. Column 1, lines 58-60. However, while the reference teaches that the first phage may be either removed or inactivated, the reference does not teach the claimed method of removing the first phage from the sample.

Olsvik teaches that the use of magnetic beads was a known method for the capture and removal of target compounds from compositions, including viruses. Page 43. The teachings of Vonk demonstrate a similar method for the detection of such viruses, where the detection also involves the capture and removal of the viruses from the sample. Because Olsvik states that the methods have proven useful in the detection of virus, and teaches that the same methods are known in the art for the removal of compounds from suspension, it would have been obvious to those in the art that these beads could be used for the removal of phage from a suspension. Therefore, it would have been obvious to those in the art that such removal would be a functional equivalent of the removal or inactivation of the phage as is taught by Wilson. Sun teaches that one method of using the beads to bind to the phage is through attaching biotin to the phage, and streptavidin to the beads such that when the two are brought into contact the phage forms a complex with the bead. See e.g., Sun et al., pages 273-74. It would therefore have been obvious to those in the art to use biotinylated phage as the first phage in the method of Wilson, and to use streptavidin coated beads for their removal. In view of these teachings, the currently claimed methods would have been obvious variants of the method described by Wilson.

With respect to claim 17, as was described above Vonk teaches a method for the detection of a virus such a is described by the steps of claim 17 relating to the capture and detection of the progeny phage. Because Vonk teaches such a method for the detection of a virus, it would have been obvious to those of ordinary skill in the art to substitute this method for the method described in Wilson for the detection of progeny phage as a functional equivalent. Both methods (the plaque assay of Wilson, and the bead immunoassay of Vonk) were described in the art as useful methods for the detection of a viral particle, and would thus have been recognized as functional substitutes for each other for such detection.

The combined teachings of these references therefore render the claimed methods obvious.

It is noted that a prior rejection over Wilson in view of a different set of secondary references was previously withdrawn in this application. See e.g., pages 3-4 of the action mailed on September 21, 2005. The withdrawal was on the basis that the claims required, and that the cited art did not teach, that the parent phage was removed from the sample after the release of the progeny phage. This limitation has been removed form the claims in view of the rejections of Madonna. Thus, the present claims do no represent an non-obvious variation from the teachings of Wilson in view of the indicated secondary references.

Conclusion

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner